Remarks

Applicant has amended the claims to more clearly point out that which is considered to be the present invention by replacing pending claims 1-46, filed in the corresponding PCT application.

Respectfully submitted,

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WE CLAIM:

Rule 1.126

47 1. A method for monitoring an effect of administration of a parathyroid hormone to a subject, comprising:

determining a level of an enzyme indicative of an osteoblastic process of bone formation, a product of collagen biosynthesis, a product of collagen degradation, or a combination thereof in a biological sample from the subject; and

correlating the level determined with an effect of administration of a parathyroid hormone.

48 2. The method of claim 47, wherein the enzyme indicative of an osteoblastic process of bone formation comprises a bone specific alkaline phosphatase.

49 3. The method of claim 48, further comprising:

determining an elevated level of the bone specific alkaline phosphatase in a period subsequent to initiation of administration of the parathyroid hormone to the subject;

correlating the elevated level of the bone specific alkaline phosphatase in the subject with a desired response to administration of the parathyroid hormone.

50 4. The method of claim 49, wherein the period subsequent to initiation of administration of the parathyroid hormone comprises a period of 0 to about 15 months after initiation of administration.

51 5. The method of claim 50, further comprising:

determining an elevated level of the procollagen I C-terminal propeptide in a period just after initiation of administration of the parathyroid hormone to the subject;

correlating the elevated level of the procollagen I C-terminal propeptide in the subject with a desired response to administration of the parathyroid hormone.

52 6. The method of claim 51, wherein the elevated level of procollagen I C-terminal propeptide correlates with the response of spinal bone mineral density to administration of the parathyroid hormone.

53 7. The method of claim 52, further comprising:

determining that the level of the procollagen I C-terminal propeptide has increased to a peak level and subsequently declined to at or near control levels in the period subsequent to initiation of administration; and

correlating the increase to a peak level and subsequent decline with the effect of the subject undergoing a desired response to administration of the parathyroid hormone.

54 8. The method of claim 47, wherein the product of collagen degradation comprises an N-telopeptide.

55 9. The method of claim 54, further comprising:

determining that the level of N-telopeptide remains substantially constant in the period just after initiation of administration; and

correlating the substantially constant level with the effect on the subject undergoing a desired response to administration of the parathyroid hormone.

56 10. The method of claim 47, wherein the subject is a woman at risk of osteoporosis.

57 11. A kit for monitoring an effect of administration of a parathyroid hormone to a subject, comprising in a container a reagent for determining a level of an enzyme indicative of an osteoblastic process of bone formation, a reagent for determining a level of a product of collagen biosynthesis, a reagent for determining a level of a product of collagen degradation, or a combination thereof; and instructions for said monitoring.

58 12. A method for using change in a biochemical marker of bone formation for predicting subsequent change in spine bone mineral density resulting from repetitive administration of a parathyroid hormone to a human subject, wherein said biochemical marker of bone formation is a product of collagen biosynthesis, said method comprising the steps of:

(a) determining the difference for said subject between the level of said biochemical marker in a biological sample taken from said subject prior to administration of said hormone and the level of said biochemical marker in a sample taken from said subject after administration of said hormone begins;

(b) comparing the difference for said subject determined in step (a) with known differences for other human subjects determined as in step (a) to find a known difference for other human subjects that is about the same as said amount of difference for said subject, wherein

said parathyroid hormone has been administered to said other human subjects under the same or similar conditions as for said subject, and

correlated amounts of subsequent change in spine bone mineral density resulting from administration of said parathyroid hormone under said same conditions are known for said known difference for other human subjects; and

(c) determining the known correlated amount of subsequent change in spine bone mineral density for said difference for said subject, thereby predicting that the subsequent change in spine bone mineral density due to said repetitive administration of a parathyroid hormone to said subject will be said known correlated amount of subsequent change in spine bone mineral density.

57 13. A method for concurrently reducing the risk of both vertebral and non-vertebral bone fracture in a male human subject at risk of or having osteoporosis, said method comprising

administering to said subject a parathyroid hormone consisting of amino acid sequence 1-34 of human parathyroid hormone

without concurrent administration of an antiresorptive agent other than vitamin D or calcium,

in a daily dose of at least about 15 μg to about 40 μg for at least about 12 months up to about 3 years.

60 14. The method of claim 13 wherein said human subject is at risk of or has osteoporosis arising from a hypogonadal condition.

61 15. The method of claim 14 wherein said hypogonadal condition is age-related.

62 16. An article of manufacture comprising packaging material and a pharmaceutical composition contained within said packaging material, said composition comprising a parathyroid hormone consisting of amino acid sequence 1-34 of human parathyroid and

said packaging material comprising printed matter which indicates that

said composition is effective for concurrently reducing the risk of both vertebral and non-vertebral bone fracture in a male human subject at risk of or having osteoporosis when administered to said subject such that said parathyroid hormone is administered

without concurrent administration of an antiresorptive agent other than vitamin D or calcium,

in a daily dose of at least about 15 μg to about 40 μg for at least about 12 months to about 3 years.